PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Kjell Bäckström et al.
Serial No. : 08/736,267
Filed : October 24, 1996
Title : COMPOSITIONS FOR INHALATION

Art Unit: 1645
Examiner: P. Duffy

Assistant Commissioner for Patents
Washington, DC 20231

DECLARATION OF KJELL BÄCKSTRÖM UNDER 37 C.F.R. § 1.132

I, Kjell Bäckström, declare:

1. I am currently the Associate Director of Explorative Pharmaceutics at Astra Draco AB, Lund, Sweden. I am a co-inventor of the subject matter of U.S. Patent Application Serial No. 08/736,267, filed October 24, 1996.

2. I am making this Declaration to provide relevant facts in support of the patentability of the subject matter claimed in the above-identified patent application.

3. I have read and understood the outstanding Office Action mailed April 28, 1998 and the references cited by the Examiner in the Office Action.

Considered 1/18/99 PAD

4. I understand that the Examiner contends that claims 1, 3-12, 17, 19-21, 26-28, 34-43, and 50-56 in the present application are anticipated by the Durrani reference (WO 91/16882).

5. I have tested C_8 diacyl phosphatidylglycerol and C_{12} diacyl phosphatidylglycerol for their ability to enhance absorption of a polypeptide in the lower respiratory tract. This

Date of Deposit October 28, 1998
I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.
Diane M. Saturno
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particular C_8 phospholipid was able to significantly enhance absorption, while this C_{12} phospholipid was not able to significantly enhance absorption. The specification at page 11, lines 18-23, states that C_8 diacyl phosphatidylcholine and C_{10} diacyl phosphatidylcholine were not effective enhancers, while a single chain phospholipid, lysophosphatidylcholine, was an effective enhancer. Thus, while the results with C_8 diacyl phospholipids were mixed, we consistently saw no absorption enhancement when the acyl groups were 10 carbons or more in length. Durrani describes certain diacyl phospholipids as useful in the formation of liposomes (see e.g., page 8, Table 1). All of Durrani's liposome-forming diacyl phospholipids have fatty acid chains of 12 carbon atoms or longer, and so are not expected to enhance absorption of a polypeptide in the lower respiratory tract.

6. I understand that the Examiner contends that claims 1, 3-12, 17, 21, 26, 27, 34-43, and 50-56 in the present application are anticipated by the Schipper reference (Pharm. Res. 10:682-686, 1993).

7. From the description of how Schipper's formulations were prepared, it is clear that the powder was obtained by freeze-drying: "The insulin solutions were then frozen in liquid N_2 and lyophilized." (page 682, col. 2, under "Preparation of Nasal Dosage Forms"). This method of preparation results in a powder consisting of relatively large particles, and not one in

which at least 50% of the particles are less than 10 microns in diameter, a size constraint necessary for efficient delivery into the lower respiratory tract. A consequent processing step, such as micronisation, is necessary to produce the smaller particles. Since Schipper does not describe such further processing (and, in fact, provides no reason to produce particles of 10 microns or smaller), Schipper does not teach the compositions of the invention.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Date: Oct 26, 1998

Kjell Bäckström

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